

Overcoming Wound Complications in Head and Neck Salvage Surgery

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“Salvage Surgery”

- Rescue oncologic surgery after prior primary treatment
 - Local-regional recurrence
 - Second Primary
 - Delayed cervical metastasis

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“Salvage Surgery”

- Revision Surgery / Complications
 - ORN
 - Hardware extrusion
 - Nonfunctional Larynx
 - Flap Revision
- Surgery in treated field
 - “Touch up” surgery
 - Aesthetic surgery

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“Salvage Surgery”

- Surgery occurring in a compromised tissue field, usually in a patient population with multiple adverse risk factors




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Growing Role of Salvage Surgery

- Rise of chemoradiation
 - “Organ Preservation” Treatment
 - VA Laryngeal Cancer Study
 - RTOG 91-11
 - Resources/Cancer Centers
- High rates of recurrence
 - ~20-30% primary
 - ~10-15% neck
- Improved Surgical Techniques

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Wound Complications

Minor	Major
Cellulitis	Free flap failure
Seroma	Major Salivary Leak/Infection
Low-flow chyle leak	High-flow chyle leak
Skin edge necrosis/dehiscence	Major soft tissue dehiscence
Minor Salivary Fistula	

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Model Example: Salvage TL


- Major wound complication rates in Salvage TL 60-80% (Johansen et al, 1988)
 - Pharyngocutaneous Fistula requiring surgery
 - Bleeding / Blowout
 - Stenosis/Stricture
- Overall complication (early + late) rates up to 90% (Sewnaik et al, 2012)

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Model Example: Salvage TL

- Longer Healing Times
- High rates of re-operation
- Longer hospitalization



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Model Example: Salvage TL

- PCF Risk Factors Meta-analysis (Dedivitis et al, 2014)
 - Previous radiation / chemoradiation
 - Diabetes mellitus
 - COPD
 - Anemia (Hgb <12.5)
 - Blood transfusion
 - Neck Dissection

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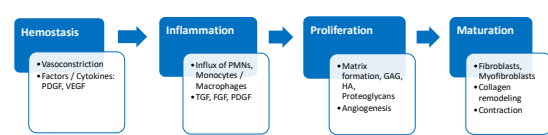
Hallmarks of Salvage Surgery

- Compromised surgical field
 - Impaired vascularity
 - Chronic tissue hypoxia
 - Altered biochemical cell function
- Compromised patient
 - Multiple adverse risk factors

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Wound Healing Biology



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    graph LR
      Hemostasis --> Inflammation --> Proliferation --> Maturation
  
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Hemostasis

- Vasoconstriction
- Factors / Cytokines: PDGF, VEGF

Inflammation

- Influx of PMNs, Monocytes / Macrophages
- TGF, FGF, PDGF

Proliferation

- Matrix formation, GAG, HA, Proteoglycans
- Angiogenesis

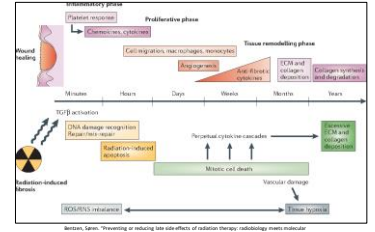
Maturation

- Fibroblasts, Myofibroblasts
- Collagen remodeling
- Contraction

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Altered Wound Healing Biology



The diagram illustrates the timeline of wound healing from minutes to years, divided into three phases: Hemostatic phase, Proliferative phase, and Tissue remodeling phase. Radiation therapy (RT) is shown to have deleterious effects on each phase:

- Hemostatic phase (Minutes):** RT causes platelet dysfunction and inhibits TGF- β activation.
- Proliferative phase (Hours to Weeks):** RT causes DNA damage, leading to impaired angiogenesis and reduced cell proliferation. It also causes vascular damage and inhibits TGF- β activation.
- Tissue remodeling phase (Months to Years):** RT causes chronic tissue hypoxia and inhibits collagen synthesis and degradation.

Berman, Sarah. "Preventing or reducing the side effects of radiation therapy: radiobiology meets molecular pathology." *Nature Reviews Clinical Oncology* 4 (2008): 309-320.

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Altered Wound Healing Biology

Acute Effects

- Hypercoagulability
- Disordered Inflammation

Late Effects

- Fibrosis
- Hypovascularity
- Blunted response to injury

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Radiation Changes

- Blood Vessel Changes**
 - Intima – thickened, dissected
 - Media – Hyalinosis, fibrosis, loss of smooth muscle cells
 - Adventitia – Fibrosis, calcification

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Radiation Changes

- Stroma / Soft Tissue Changes**
 - Excess collagen deposition
 - Diminished density and size of blood vessels

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Impact of Radiation

- Dose dependence**
 - ↑ flap failure, local complications, hematoma with >60Gy (Benetar et al. 2003)
 - ↑ flap failure, hardware exposure, fistula requiring surgery, need for 2nd flap in patients with multiple rounds of XRT (Gordin and Ducic 2015)

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Impact of Radiation

- Timing after Radiotherapy**
 - Chronic radiation changes (hypercoagulability and fibrosis) takes months to manifest
 - 36% overall complications >4months vs 14% <4months (Bengtson et al, 1993)
 - ↑ healing complication rate with <4, 4-6, >6 weeks post-XRT (Halle et al, 2009)
 - ↑ free flap failure rate with < 6 weeks, 6-15 weeks, >15 weeks (Tall et al, 2015)

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Not Just Radiation

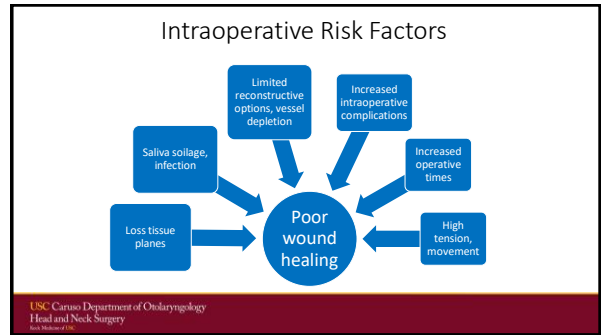
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Factors Inhibiting Wound Healing	
Local	Systemic
Poor Blood supply	Advanced age
Tissue Hypoxia	Malnutrition
Microorganisms/Infection	Chemotherapy
Foreign body	Radiotherapy
Nonviable tissue	Immunosuppression
Tension/mobility	Stress states
Malignancy	Drugs/corticosteroids
	Endocrinopathy
	Smoking and alcohol
	Obesity
	Other systemic disease (connective tissue disorders, metabolic disorders, vasculopathies, etc)

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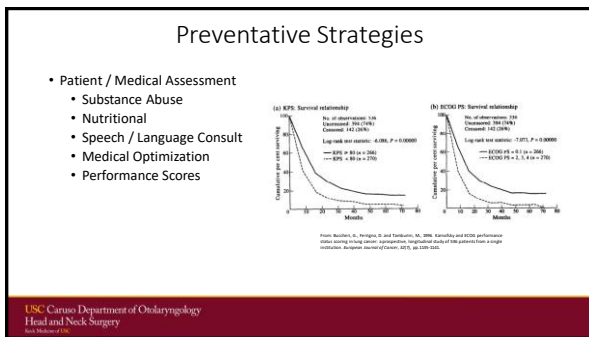
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Preventative Strategies

- Planning / Selection
 - Consider additional or advanced imaging
 - Multidisciplinary tumor board
 - Palliative Care

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Preventative Strategies

- Operative Factors
 - Antibiotic prophylaxis
 - Incision planning
 - +/- Neck dissection
 - Staged surgery

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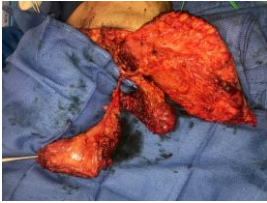
Preventative Strategies

- Operative Factors
 - Use of vascularized free tissue
 - "The irradiated patient" definitively represents a complex clinical entity in which the surgical outcome is actually related to the radiotherapy/CRT effects themselves, as well as to a number of secondary changes that may be directly or indirectly linked to such a preoperative treatment. In this light: free tissue transfer should not be considered as an adjunctive procedure that simply adds risk to ablative surgery, but as a way (and probably the best one, at the moment) to improve wound healing in an already unfavorable scenario." (Paderno et al, 2016)

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Preventative Strategies



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Preventative Strategies



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Preventative Strategies

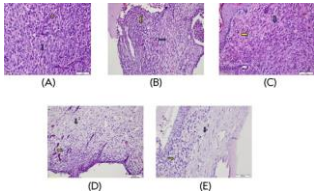


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Preventative Strategies

- Targeted Therapies
 - Prostaglandin E1 infusions
 - Plasma Rich Protein
 - Fibrin glue



Miyahara A, Shimizu A, Saitoh C, Ogino Y, Nakano O, Ohno K, et al. Can tissue adhesion and plasma rich protein prevent pharyngocutaneous fistula formation? *Ann Surg Oncol*. 2016;23(12):1517-22.

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Preventative Strategies

- Post-operative Management
 - Consider prolonged antibiotic course
 - Surgical Drain Management
 - HOB elevation to reduce edema
 - Aggressive nutrition support

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Dealing with Wound Complications

- Optimize Wound Environment
 - Lower Bacterial Count
 - Quantitative / Qualitative Culture
 - Dakin's, silver-based dressings, antibio
 - Debridement, dressing changes
 - Topical Treatments
 - Hydrocolloids
 - Alginates
 - Enzymes



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Dealing with Wound Complications

- Optimize Wound Environment
 - Divert salivary contamination
 - Bypass drains, Malecot catheter
 - Formalize fistula



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Dealing with Wound Complications

- Negative Pressure Wound Vacuum
 - Speeds wound closure
 - Shortened hospitalization
 - Decreased patient discomfort/morbidity



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Dealing with Wound Complications

- Hyperbaric Oxygen Therapy
 - Increases tissue oxygen saturation
 - Promotes angiogenesis
 - Reverses cellular ischemia
 - Oxygen Free Radicals
 - Antimicrobial
 - Reduces Tissue Edema



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Dealing with Wound Complications

Cochrane Database of Systematic Reviews
Hyperbaric oxygen therapy for late radiation tissue injury
Cochrane Systematic Review - Intervention | Version published: 28 April 2016 [see what's new](#)

- Hyperbaric Oxygen Therapy
 - Improved outcomes in:
 - Bony and soft tissue wounds of head and neck
 - Prevention of ORN in dental extraction
 - Adjuvant use with Free Flap Reconstruction

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Dealing with Wound Complications

- Vascularized tissue coverage
 - Muscle (Rectus, Pectoralis, Latissimus)
 - Highly vascular
 - Conforms and fills dead-space
 - Expresses growth factors

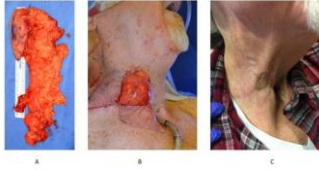


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Dealing with Wound Complications

- Vascularized tissue coverage
 - Gastro-omentum
 - Supply of fibroblasts and stem cells
 - Highly vascular and pliable



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Conclusion

- "Salvage surgery" = unfavorable local + systemic risk factors
- Lack of guidelines
- Proactive intervention
- Free tissue transfer is the standard of reconstruction

Factors Inhibiting Wound Healing	
Local	Systemic
Poor Blood supply	Advanced age
Tissue Hypoxia	Malnutrition
Microorganisms/Infection	Chemotherapy
Foreign body	Radiotherapy
Nonviable tissue	Immunosuppression
Tension/mobility	Stress states
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	Obesity
	Other systemic disease
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Questions?



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